IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants:	Solomon S. Steiner and Bryan R. Wilson		
Serial No.:	09/766,362	Art Unit:	1615
Filed:	January 19, 2001	Examiner:	Humera Sheikh
For:	*DRY POWDER FORMULATIONS OF ANTIHISTAMINE FOR NASAL ADMINISTRATION*		

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF TO EXAMINER'S ANSWER

Sir:

This is a reply brief to the Examiner's Answer mailed March 23, 2006, in the above-referenced application. Submitted with this Reply Brief is a Request for Oral Hearing. A Reply Brief and a Request for an Oral Hearing, along with the required fee, were previously filed with the U.S. Patent and Trademark Office on July 20, 2005. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

(8) ARGUMENT

Appellants affirm all of the arguments made in the Appeal Brief.

Contrary to the Examiner's assertion on page 8 of the Examiner's Answer mailed March 23, 2006, the limitation in claim 1, "in a form suitable for nasal administration" is a functional limitation, not a "future intended use." M.P.E.P. § 2173.05 (g) defines functional limitations and explains that they "must be evaluated and considered, just like any other limitation of the claim." *Id.* Therefore, the Examiner should have considered this limitation in his analysis of the patentability of the claims.

Steiner notes that drugs may be administered topically in the form of an ointment or cream (*see* col. 13, lines 1-2), a solution or suspension for parenteral, intradermal or subcutaneous administration (*see* col. 11, lines 50-51), or may be in an oral dosage form, such as in the form of a tablet, pill, capsule or troche (*see* col. 11, lines 66 until col. 12, line 1). None of these forms are suitable for nasal administration. As noted in the Appeal Brief, the only reference to the nasal tract occurs when Steiner mentions that microparticles can include a diagnostic imaging agent useful for imaging the nasal tract (col. 13, lines 17-21). However, Steiner does not disclose the form in which the microparticles are administered to image the nasal tract. In contrast, Steiner lists a number of different dosage forms which are not suitable for nasal administration. For example, formulations that are suitable for injection are administered in solution, in a volume that suspends the particles so that they are readily distributed at the site of administration. In contrast, a formulation suitable for nasal

administration cannot be suspended in a quantity of liquid since this would wash away the particles from the site of deposition. Additionally, formulations for oral administration are in the form of a tablet or capsule, which is not a form suitable for nasal administration. Further, Steiner does not suggest modifying the formulations to make them suitable for nasal administration. Therefore claim 1 and its dependent claims, claims 2, 4, and 5, are non-obvious in view of Steiner.

Independent claims 7 and 14 each contain a limitation that is similar to the limitation in claim 1 discussed above. Claim 7 specifies that the dry powder is "in a dosage formulation for administration to the nasal region". Claim 14 specifies that the dry powder is "suitable for nasal administration". These are also functional limitations. As noted above with respect to claim 1 and its dependent claims, Steiner does not disclose or suggest "microparticles in a dosage formulation suitable for administration to the nasal region" or a "dry powder suitable for nasal administration". Therefore claim 7 and its dependent claims, claims 9 and 12, and claim 14 and its dependent claims, claims 15, 17 and 18, are non-obvious over Steiner.

Claims 7, 9 and 12 are non-obvious over Steiner

Independent claim 7 and its dependent claims define a drug delivery device for nasal administration. Claim 7 specifies that the device contains a device for delivering a measured dose of the drug to the nasal mucosa. Steiner does not disclose or suggest a device for delivering a measured dose of a drug to the nasal mucosa. The only drug delivery devices disclosed by Steiner are ampoules, disposable syringes, and multiple dose vials made of glass or plastic,

which are suitable for delivering a drug parenterally (*see* col. 11, lines 60-63). Steiner notes that drugs may be administered topically in the form of an ointment or cream (*see* col. 13, lines 1-2) or may be injected subcutaneously, intramuscularly or into the peritoneum using a standard gauge needle (*see* col. 12, lines 43-52). None of the devices or methods of administration are suitable for delivering a measured dose of the drug to the nasal mucosa, as required by claim 7 and its dependent claims. Further Steiner does not suggest using a device for administering a drug to the nasal mucosa. Therefore, claims 7, 9, and 12 are non-obvious over Steiner.

Claims 14, 15, 17, and 18, are non-obvious over Steiner

Independent claim 14 and its dependent claims define a method for administering a drug to the nasal region of a patient. Claim 14 specifies that the method requires nasally administering a dry powder suitable for nasal administration. Steiner does not disclose or suggest nasally administering a dry powder. Steiner discloses a variety of other methods of administration, such as oral administration (*see* col. 11, line 66 until col. 12, line 4), topical administration of an ointment or cream (*see* col. 12, line 60 until col. 13, line 2), and parenteral administration (*see* col. 11, lines 61-63). As noted in the Appeal Brief, the only reference to the nasal tract occurs when Steiner mentions that microparticles can include a diagnostic imaging agent useful for imaging the nasal tract. However, Steiner does not disclose the form in which the microparticles are administered to image the nasal tract. Further, Steiner does not suggest nasal administration of a dry powder. Therefore, claims 14, 15, 17, and 18 are non-obvious over Steiner.

Claims 3, 8, 10, 16, 20, and 21 are non-obvious over Steiner in view of Illum

The Examiner has not considered the references as a whole in his analysis of the pending claims. The Examiner argues that Illum simply discloses the administration of antihistamines for nasal applications. However, one of skill in the art would not combine the antihistamines of Illum with the drug delivery system of Steiner. Even if they were combined, the combination would not result in the compositions, devices, and methods defined by the claims for the reasons noted in the Appeal Brief and discussed below.

There is no teaching to combine Steiner and Illum

Illum describes bioadhesive microspheres that form a gel upon contact with nasal mucosa (col. 3, lines 2-9 and col. 6, lines 13-15). Illum lists a number of suitable materials for forming the microspheres. All of the listed materials are polymers, such as starch, gelatin, casein, dextrans, alginate, agarose, albumin, collagen, chitosan, polyvinylacetate, and hyaluronic acid esters (col. 6, lines 15-19). Illum does not disclose a non-polymeric material that does not form a gel when placed on mucosal surfaces, such as a diketopiperazine.

Illum emphasizes the importance of gel-forming, bioadhesive systems. These microparticles allow for an increased period of contact with the mucosal surface in the nasal cavity (*see* col. 5, lines 19-23 and col. 8, lines 49-51). Thus, Illum teaches away from using microparticles that do not form gels.

Further, Illum does not disclose or suggest that the microspheres should have a narrow size range, let alone the claimed size range of 10-20 microns. Illum's microspheres have a broad

size range, with diameters ranging from 10 microns to 100 microns (col. 6, lines 13-14). Illum discloses different methods for making the polymeric microspheres, which generally result in the formation of microspheres outside of the claimed size range. For example, Illum discloses forming starch microspheres having a mean size of 33 microns (col. 6, lines52-53); albumin microspheres having a size in the range of 40-60 microns (col. 7, lines 1-2) and a mean size of 43 microns ± 6 microns (col. 7, lines 19-20); gelatin microspheres, having a mean particle size of 70 microns (col. 7, lines 30-31) and 60 microns ± 6 microns (col. 7, lines 41-42); and chitosan microspheres having a broad size range from 10-90 microns (col. 7, lines 53-54). Additionally, although Illum notes that acceptable diameters range for 10 microns to 100 microns, the particles formed by the methods disclosed by Illum generally tend to be larger than 20 microns.

In contrast, Steiner discloses microparticles formed of diketopiperazines and an encapsulated drug. Steiner does not disclose or suggest using gel-forming polymers in its drug delivery system. Further, Steiner discloses administering small microparticles, with average diameters between 0.1 and 10 microns (col. 4, lines 39-40), while Illum focuses on the administration of larger particles. Therefore there is no suggestion in Steiner or Illum to combine these references; and claims 3, 8, 10, 16, 20, and 21 are non-obvious.

The combination of Steiner and Illum

Even if one of ordinary skill in the art combined Steiner with Illum, the claimed compositions, devices, and methods would not be obvious. As noted above, Steiner focuses on the delivery of small microparticles, having a size ranging from 0.1 to 10 microns, while Illum

discloses the administration of larger microparticles having a broad range of sizes, *i.e.* from 10 to 100 microns. Additionally the methods provided in Illum are generally used to form large particles, having diameter greater than 20 microns. The combination of Steiner with Illum does not disclose or suggest the selection of microparticles having a narrow size range of between 10 microns and 20 microns, as required by the claims.

As noted in the Appeal Brief, the dry powder formulations defined by the claims reduce the systemic side effects associated with liquid nasal sprays because the drug is maintained in the nasal cavity (page 2, lines 2-3). This result is achieved through the selection of microparticles having an average particle size of between 10 and 20 microns (page 3, lines 5-10). These microparticles are retained in the nasal region and do not pass into the pulmonary system or the mouth. Particles smaller than 10 microns could cause the composition to pass into the pulmonary region or mouth, resulting in less efficient delivery of the drug and causing undesirable side effects with certain type of drugs, e.g., bitterness in the case of an antihistamine. In addition, since the particles as defined by the claims are retained in the nasal region, lower doses of drug can be administered (page 2, lines 23-26). Neither Steiner nor Illum disclose or suggest microparticles having a size of between 10 and 20 microns. Thus, claims 3, 8, 10, 16, 20, and 21 are non-obvious in view of the combination of Steiner and Ilum.

(9) SUMMARY AND CONCLUSION

For the foregoing reasons and those in the Second Substitute Appeal Brief filed December 27, 2005, Appellants submit that claims 1-5, 7-12, and 14-21 are non-obvious.

Respectfully submitted,

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